

WHAT IS CLAIMED IS:

1. A blood coagulation factor IX-activating protein derived from a mammal, which has an amino acid sequence of SEQ ID NO.4 and has the following properties:

(1) the protein acts on blood coagulation factor IX to activate said factor;

(2) the activity of the protein is inhibited in the presence of an α 1-protease inhibitor or soybean trypsin inhibitor;

(3) the protein is present in erythrocyte membrane;

(4) the protein has a molecular weight of approximately 29 kDa as measured by SDS-PAGE.

2. The blood coagulation factor IX-activating protein according to claim 1 which cuts the amino acid sequence of the blood coagulation factor IX between 140th threonine and 141th serine, between 181th valine and 182th valine, and between 182th valine and 183th glycine.

3. The blood coagulation factor IX-activating protein according to claim 1 which is derived from human.

4. The blood coagulation factor IX-activating protein according to claim 1 which is purified by disrupting erythrocytes, extracting with a surfactant, and subjecting the extract to anion exchange chromatography and heparin affinity chromatography.

5. A medicine which comprises a blood coagulation factor IX-activating protein according to claim 1.

6. The medicine according to claim 5 which is used for treatment and/or prevention of diseases associated with abnormal blood coagulation.

7. An agent for activating blood coagulation factor IX which comprises a blood coagulation factor IX-activating protein of claim 1.

8. An antibody or fragment thereof which recognizes a blood coagulation factor IX-activating protein of claim 1.

9. The antibody or fragment thereof according to claim 9 wherein the antibody is a monoclonal antibody.

10. A medicine which comprises an antibody or fragment thereof

of claim 8.

11. The medicine according to claim 10 which is used for treatment and/or prevention of diseases associated with abnormal blood coagulation.

12. A labeled antibody or fragment thereof which recognizes a blood coagulation factor IX-activating protein of claim 1.

13. A medicine which comprises a labeled antibody or fragment thereof of claim 12.

14. The medicine according to claim 14 which is a diagnostic drug for diseases associated with blood coagulation.

15. A method for detecting a blood coagulation factor IX-activating ability which comprises detecting or measuring a blood coagulation factor IX-activating protein of claim 1 in a biological sample.

16. A method for evaluating a risk of blood coagulation in a subject with diabetes, pregnancy or aging, which comprises a step of determining the degree of activation of a blood coagulation factor IX by the blood coagulation factor IX-activating protein of claim 1 in erythrocytes in a subject.

17. The method according to claim 16 wherein the degree of activation of a blood coagulation factor IX is determined by determining the time of onset of coagulation of a mixture of erythrocytes (RBCs) and platelet free plasma (PFP) which was prepared from a blood of a subject. ✓

18. A peptide consisting of an amino acid sequence from 141th serine to 181th valine of a blood coagulation factor IX.

19. The peptide according to claim 18 which is obtained by treating a blood coagulation factor IX with the blood coagulation factor IX-activating protein according to claim 1.

20. A method for screening an inhibitor for the blood coagulation factor IX-activating protein according to claim 1, wherein said the blood coagulation factor IX-activating protein is used.

21. The method according to claim 20, wherein a fluorogenic synthetic substrate, the blood coagulation factor IX-activating protein according to claim 1 and a candidate inhibitor are mixed

and incubated, and then the fluorescence intensity is measured.

22. The method according to claim 21, wherein the fluorogenic synthetic substrate is Suc(OMe)-Ala-Ala-Pro-Val-MCA.

23. A method for inhibiting the activation of a blood coagulation factor IX by the blood coagulation factor IX-activating protein according to claim 1, wherein the inhibitor which is obtained by the method of according to any of claims 20 to 22 is used.

24. A method for analyzing the activity of the blood coagulation factor IX-activating protein of claim 1 which comprises steps of (a) providing a substrate which can not be cleaved with esterase but can be cleaved with the blood coagulation factor IX-activating protein of claim 1, and which is obtained by substituting the amino acid(s) of the cleavage site of a blood coagulation factor IX which is cleaved by esterase only, with another amino acid(s); (b) reacting the substrate with the blood coagulation factor IX-activating protein of claim 1; and (c) detecting the substrate which was cleaved with the blood coagulation factor IX-activating protein of claim 1.